OCT and HVF Makes Glaucoma Easy: Cases that Beg to Differ

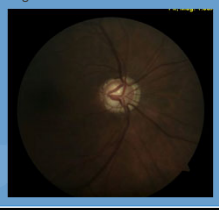
David Fleischman, MD, MS, FACS
Perioperative Medical Director, UNC Hillsborough
Associate Professor
Director, Glaucoma Fellowship
Director, Ocular Trauma
University of North Carolina at Chapel Hill

Disclosures

- Optopol, Inc (PI)

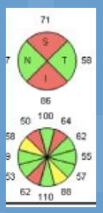
Define… Glaucoma

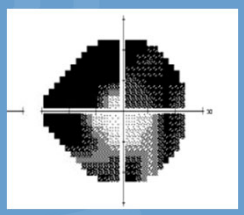
- What is glaucoma?
  - An IOP-dependent eye disease that may result in vision loss
    - Typical features:
      - Regional atrophy
      - Corresponding visual field changes



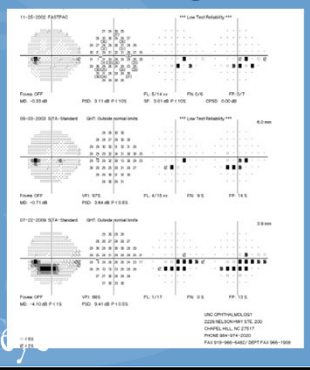
Pattern Recognition

- Superior and Inferior Thinning
- Typical Visual Field Loss





Pattern Recognition



Pattern Recognition

- Intraocular pressures
  - Are they on glaucoma meds already?
- Corneal thickness
  - Ensure no corneal edema
- Older age
- Race (depending on form of glaucoma)
- Family history

Rapid Fire Cases

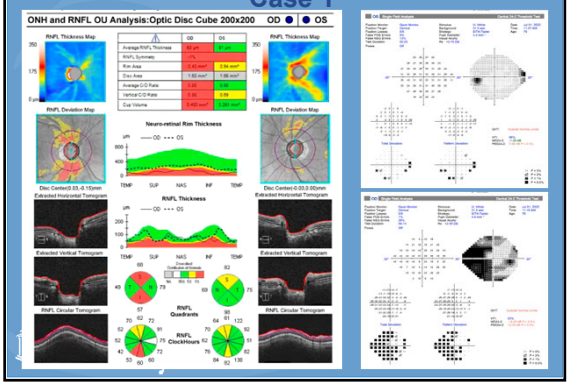
UNC eye

Case 1

- 79-year-old White male
- Negative family history
- Denies trauma, steroid use
- Tmax: OD: 25 mm Hg OS: 15 mm Hg
- CCT: 548 µm : 558 µm
- Gonio: SS 360 both eyes

UNC eye

Case 1



Case 1 Synopsis

- Primary open angle glaucoma, asymmetric

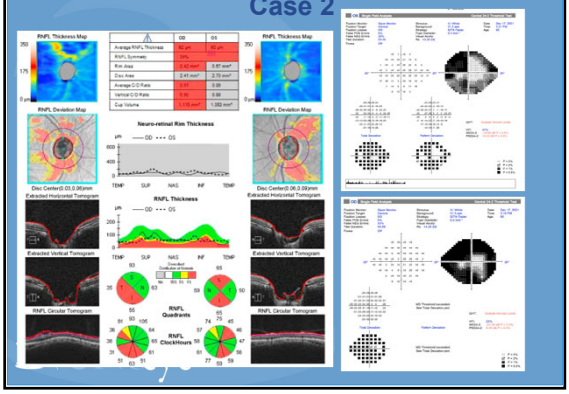
UNC eye

Case 2

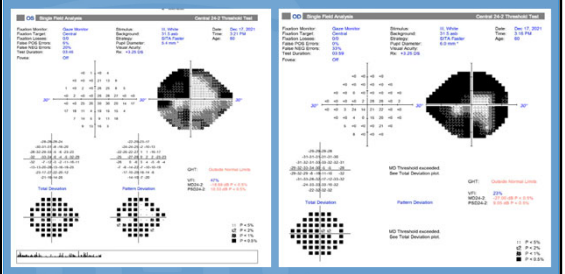
- 61-year-old Black male
- Negative family history
- Denies trauma, steroid use
- Tmax: OD: 45 mm Hg OS: 38 mm Hg
- CCT: 518 µm : 522 µm
- Gonioscopy: PTM/SS 360 OU

UNC eye

Case 2



Case 2



UNC eye

Case 2 Synopsis

- MRI: remote right temporal infarct
- Primary open angle glaucoma, asymmetric
  - Glaucoma is allowed to co-exist with other disease processes
  - Clue in on depth of visual field defect

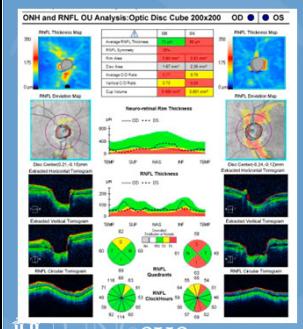
UNC eye

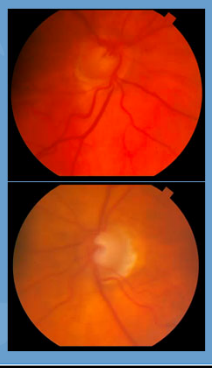
Case 3

- 92-year-old White male
- Unknown family history
- Denies trauma, steroid use
- TMax: OD: 25 mm Hg OS: 27 mm Hg
- CCT: 564 µm : 533 µm
- Gonioscopy: CBB 360 (prior to CE/IOL in 2010)
- Notable: pseudoexfoliation syndrome, more evident on left eye than right eye

UNC eye

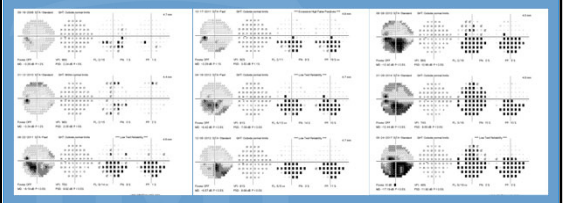
Case 3





UNC eye

Case 3



UNC eye

Case 3 Synopsis

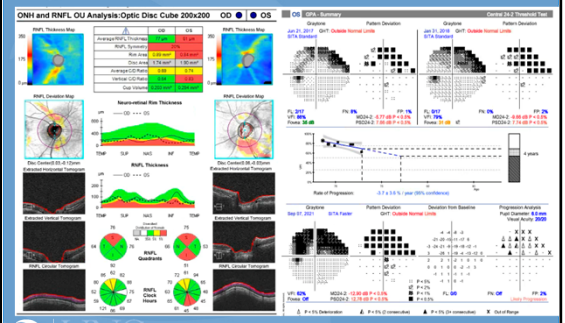
- Pseudoexfoliation glaucoma

UNC eye

Case 4

- 73-year-old White female
- Family history: brother, nephew
- Denies trauma, steroid use
- TMax: 15 mm Hg both eyes
- CCT: 561 µm and 547 µm
- Gonioscopy: CBB 360 both eyes
- Color Plates: 11 out of 11 both eyes

Case 4

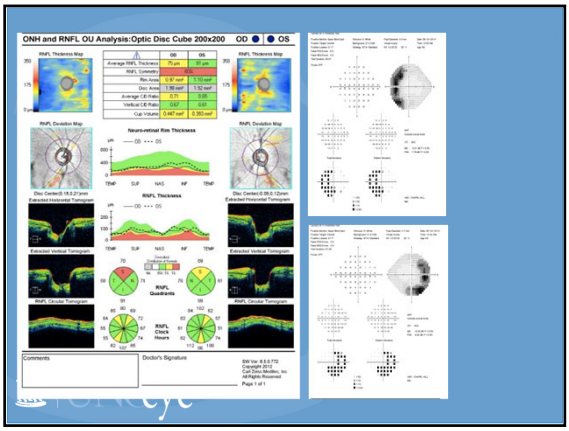


Case 4 Synopsis

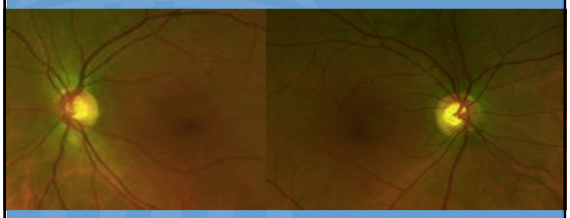
- Primary open angle glaucoma
  - Note typical advancement of visual field defects over time
  - Be skeptical of very fast visual field changes, especially at low-normal pressures

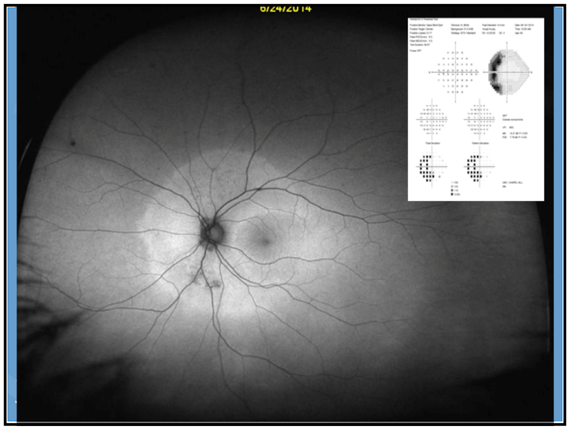
Case 5

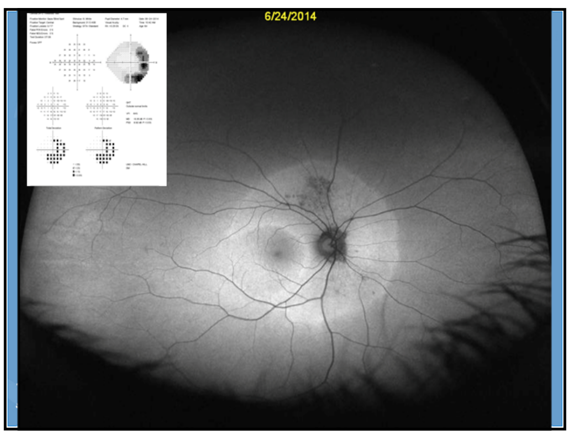
- 72-year-old White female
- Family history: unknown (adopted)
- Denies trauma, steroid use
- TMax: OD: 15 mm Hg OS: 16 mm Hg
- CCT: 522 µm and 521 µm
- Gonioscopy: CBB 360 both eyes
- Color Plates: 6 out of 6 Ishihara bilaterally

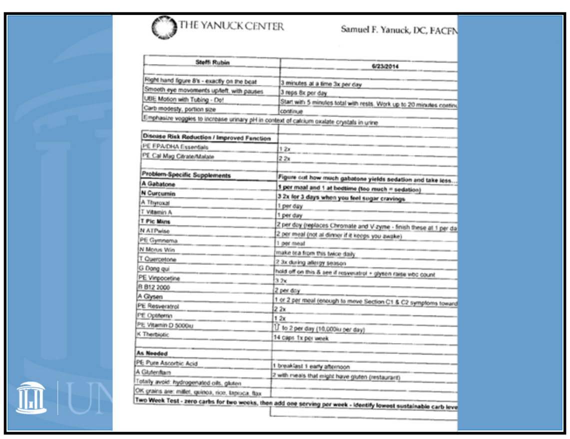


Case 5









THE YANUCK CENTER

Samuel F. Yanuck, DC, FACFN

Steffi Rubin	6/23/2014
Right hand figure 8's - exactly on the beat	3 minutes at a time 3x per day
Smooth eye movements up/left, with pauses	3 reps 8x per day
UBE Motion with Tubing - Do!	Start with 5 minutes total with rests. Work up to 20 minutes contin
Carb modesty, portion size	continue
Emphasize veggies to increase urinary pH in context of calcium oxalate crystals in urine	
Disease Risk Reduction / Improved Function	
PE EPA/DHA Essentials	1 2x
PE Cal Mag Citrate/Malate	2 2x
Problem-Specific Supplements	**Figure out how much gabatone yields sedation and take less...**
A Gabatone	**1 per meal and 1 at bedtime (too much = sedation)**
N Curcumin	**3 2x for 3 days when you feel sugar cravings**
A Thyroxal	1 per day
T Vitamin A	1 per day
T Pic Mins	2 per day (replaces Chromate and V-zyme - finish these at 1 per da
N ATPwise	2 per meal (not at dinner if it keeps you awake)
PE Gymnema	1 per meal
N Morus Win	make tea from this twice daily
T Quercetone	2 3x during allergy season
G Dong qui	hold off on this & see if resveratrol + glysen raise wbc count
PE Vinpocetine	3 2x
B B12 2000	2 per day
A Glysen	1 or 2 per meal (enough to move Section C1 & C2 symptoms toward
PE Resveratrol	2 2x
PE Optiferrin	1 2x
PE Vitamin D 5000iu	1 to 2 per day (10,000iu per day)
K Therbiotic	14 caps 1x per week
As Needed	
PE Pure Ascorbic Acid	1 breakfast 1 early afternoon
A Glutenflam	2 with meals that might have gluten (restaurant)
Totally avoid: hydrogenated oils, gluten	
OK grains are: millet, quinoa, rice, tapioca, flax	
Two Week Test - zero carbs for two weeks, then add one serving per week - identify lowest sustainable carb leve	

	Support right cerebellar function
	Support cellular remapping and left cortex function
continuous. Larger L arm circle	
less...	
	(support healthy modulation of insulin release)
	(support healthy modulation of NFkB loop)
	(support healthy thyroid function)
	(support healthy thyroid receptor function)
per day each)	(support healthy insulin receptor sensitivity)
	(support healthy metabolism)
	(support healthy metabolism)
	(support healthy modulation of histamine release)
	(support healthy blood)
	(support healthy small vessel circulation)
	(support healthy B12 levels)
toward zero)	(support healthy blood sugar balance)
	(support healthy iron levels)
	(anti-inflammatory, immune modulator)
	(probiotic)
	(adrenal support)
	(repair GI mucosa)
rb level.	

Case 5

Cytotoxic Effects of Curcumin in Human Retinal Pigment Epithelial Cells

Margrit Hollborn[1]*, Rui Chen[1], Peter Wiedemann[1], Andreas Reichenbach[2], Andreas Bringmann[1], Leon Kohen[1,3]

1 Department of Ophthalmology and Eye Hospital, University of Leipzig, Leipzig, Germany, 2 Paul Flechsig Institute of Brain Research, University of Leipzig, Leipzig, Germany, 3 Helios Klinikum Aue, Aue, Germany

Abstract

Backround: Curcumin from turmeric is an ingredient in curry powders. Due to its antiinflammatory, antioxidant and anticarcinogenic effects, curcumin is a promising drug for the treatment of cancer and retinal diseases. We investigated whether curcumin alters the viability and physiological properties of human retinal pigment epithelial (RPE) cells *in vitro*.

Methodology/Principal Findings: Cellular proliferation was investigated with a bromodeoxy-uridine immunoassay, and chemotaxis was investigated with a Boyden chamber assay. Cell viability was determined by trypan blue exclusion. Apoptosis and necrosis rates were determined with a DNA fragmentation ELISA. Gene expression was determined by real-time PCR, and secretion of VEGF and bFGF was examined with ELISA. The phosphorylation level of proteins was revealed by Western blotting. The proliferation of RPE cells was slightly increased by curcumin at 10 μM and strongly reduced by curcumin above 50 μM. Curcumin at 50 μM increased slightly the chemotaxis of the cells. Curcumin reduced the expression and secretion of VEGF under control conditions and abolished the VEGF secretion induced by PDGF and chemical hypoxia. Whereas low concentrations of curcumin stimulated the expression of bFGF and HGF, high concentrations caused downregulation of both factors. Curcumin decreased dose-dependently the viability of RPE cells via induction of early necrosis (above 10 μM) and delayed apoptosis (above 1 μM). The cytotoxic effect of curcumin involved activation of caspase-3 and calpain, intracellular calcium signaling, mitochondrial permeability, oxidative stress, increased phosphorylation of p38 MAPK and decreased phosphorylation of Akt protein.

Conclusion: It is concluded that curcumin at concentrations described to be effective in the treatment of tumor cells and in inhibiting death of retinal neurons (~10 μM) has adverse effects on RPE cells. It is suggested that, during the intake of curcumin as concomitant therapy of cancer or in the treatment of eye diseases, retinal function should be monitored carefully.

Citation: Hollborn M, Chen R, Wiedemann P, Reichenbach A, Bringmann A, et al. (2013) Cytotoxic Effects of Curcumin in Human Retinal Pigment Epithelial Cells. PLoS ONE 8(3): e59603. doi:10.1371/journal.pone.0059603

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Competing Interests: The authors have declared that no competing interests exist.

* E-mail: hollbm@medizin.uni-leipzig.de

Case 5

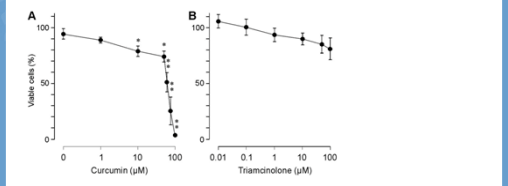


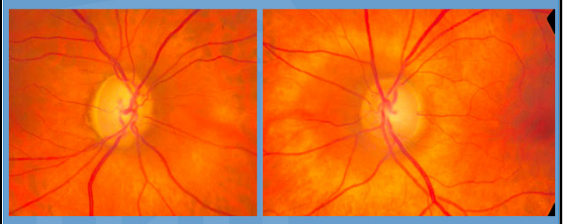
Figure 4. Concentration-dependent effects of curcumin (A) and triamcinolone acetonide (B) on the viability of RPE cells. The percentage of viable cells was evaluated 24 h after addition of the test substances to the culture medium. Data are means ±; SEM of 5–7 independent experiments carried out in triplicate using cells from different donors, and are expressed in percent of untreated control (100%). Significant difference vs. control: *P<0.05; **P<0.01.
doi:10.1371/journal.pone.0059603.g004

Case 6

- 77-year-old White female
- Family history: mother
- Denies trauma, steroid use
- TMax: OD: 33 mm Hg and OS: 22 mm Hg
- CCT: 558 µm and 556 µm
- Gonioscopy: open prior to CE/IOL
- Status post trabeculectomy in 2011
- Notable: pigment dispersion syndrome, +/- low tension glaucoma equivalent

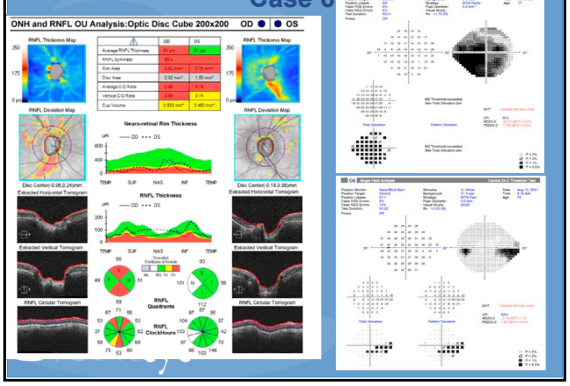
UNC eye

Case 6

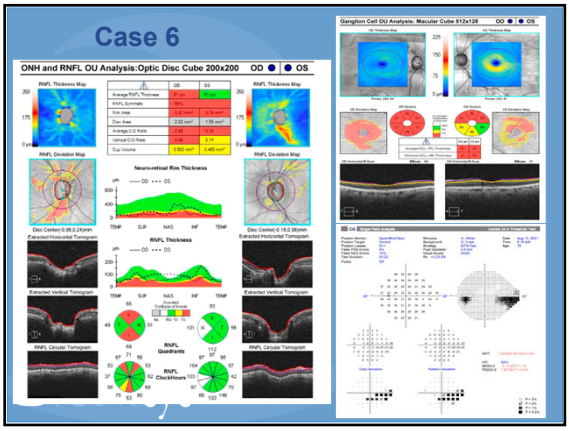


UNC eye

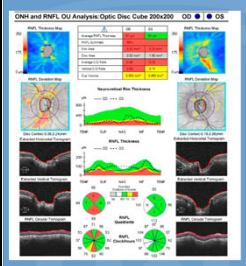
Case 6

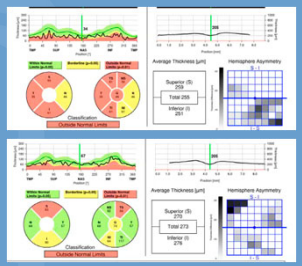


Case 6



Case 6





UNC eye

Case 6 Synopsis

- Pigmentary Glaucoma
  - Highly elevated intraocular pressures can result in necrotic cell death with glialization of the nerve
  - Tends to burn out with time (affecting visual field and OCT progression)
  - However, can develop low-tension glaucoma equivalent state

UNC eye

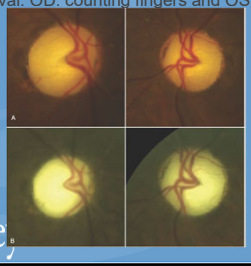
Case 7

- 76-year-old Black male
- Family history: maternal aunt, maternal cousin
- Denies trauma, steroid use
- TMax: 17 mm Hg both eyes
- CCT: 523 µm; 527 µm
- Gonioscopy: SS 360
- History of pituitary macroadenoma: s/p resection in 2009, 2nd resection in 2012; radiotherapy in 2012 (51.24 Gy)

UNC eye

Case 7

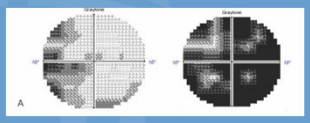
- On exam:
  - The patient's visual acuity was 20/400 OD and 20/200 OS on initial eval
  - Current eval: OD: counting fingers and OS: counting fingers



UNC eye

Case 7

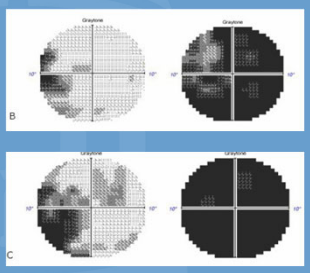
- Visual Fields:



UNC eye

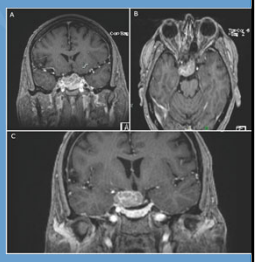
Case 7

- Visual Fields:

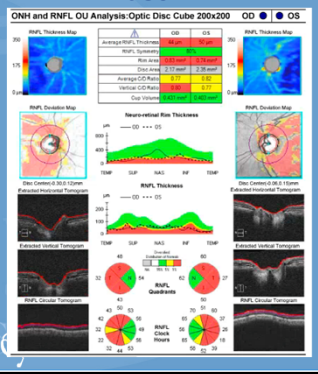


Case 7

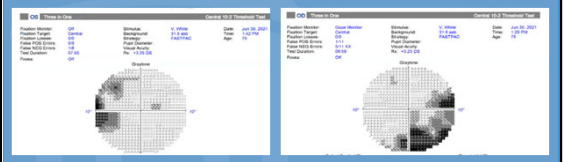
- MRI (2017) Impression: "similar size and appearance of residual enhancing suprasellar mass with optic chiasm compression."
- **Neurosurg Eval**: "Stable mass, not growing. Unlikely to be causing recent changes in vision."



Case 7



Case 7



Follow up visit: OD: 20/400 and OS: 20/200

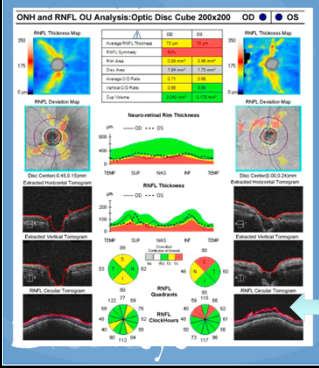
Case 7 Synopsis

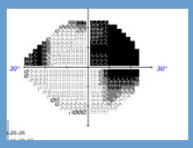
- Compression is compression, even if stable
  - Trabs don't treat tumors
  - Again, be skeptical of progression at very low intraocular pressures

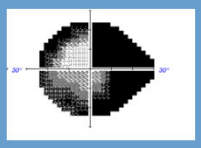
Case 8

- 54-year-old Black male
- Family history: negative
- Denies trauma, steroid use
- TMax: 23 mm Hg right eye, 46 mm Hg left eye
- CCT: 555 µm ; 548 µm
- Gonioscopy: ciliary body 360, both eyes
- Notable: proliferative diabetic retinopathy; no evidence of NVI/NVA/PAS; has had vitrectomy for non-clearing vitreous hemorrhage (left eye)

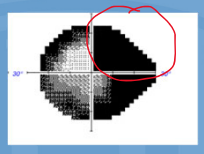
Case 8

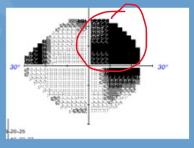






Case 8





June 2021: Left parafalcine subdural hematoma secondary to head injury….

… and glaucoma.

UNC eye

Case 8 Synopsis

- Buried visual field defects:
  - Really, be on the look-out!
- Proliferative diabetic retinopathy, epiretinal membranes, dynamic hyaloid interfaces can affect RNFL thickness or create difficulty in segmenting the retinal nerve fiber layer

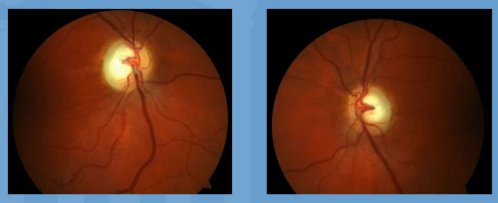
UNC eye

Case 9

- 30-year-old White female
- Family history: father, paternal grandmother
- Denies trauma, steroid use
- TMax: 18 mm Hg and 19 mm Hg on Betimol (unknown Tmax without meds)
- CCT: 532 µm : 522 µm
- Gonioscopy: CBB 360 both eyes
- Color Plates: 10/11 both eyes
- Notable: Congenital nystagmus

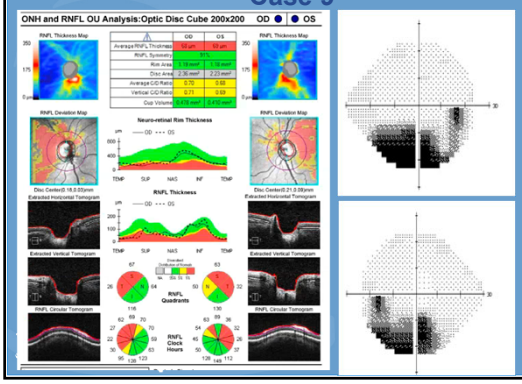
UNC eye

Case 9



UNC eye

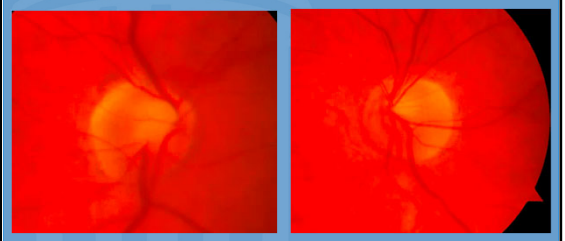
Case 9

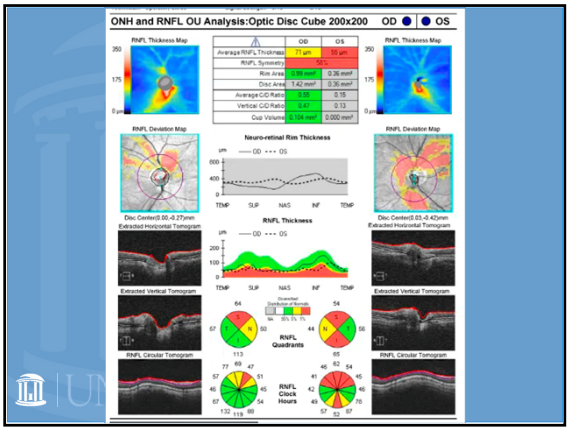


Supplemental Case 9

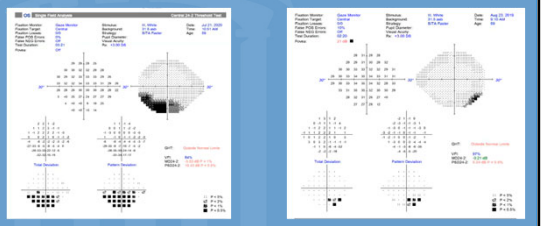
- 62 year-old White female
- Family history: negative
- Denies trauma, steroid use
- TMax: 18 mm Hg and 19 mm Hg
- CCT: 578 µm and 565 µm
- Gonioscopy: open to SS 360 prior to CE/IOL

Case 9+





Case 9+



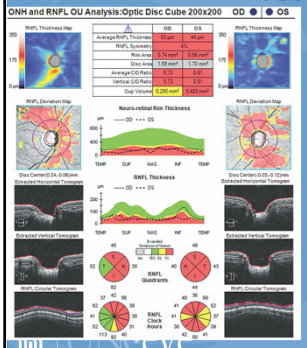
Case 9/9+ Synopsis

- Maldevelopment of the optic nerve
- Superior segmental optic nerve hypoplasia
  - Can still co-exist with glaucoma
  - Note typical pattern of visual field loss

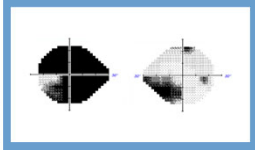
Case 10

- 36-year-old White female
- Family history: maternal grandmother
- Denies trauma, steroid use
- TMax: 14 mm Hg both eyes
- CCT: 522 µm and 519 µm
- Gonioscopy: CBB 360 both eyes
- Color plates: 12 out of 12 both eyes
- Notable: presented to ENT for sensorineural hearing loss, left-sided weakness and pain; referred to ophthalmology when there was concern for possible multiple sclerosis and/or glaucoma

Case 10

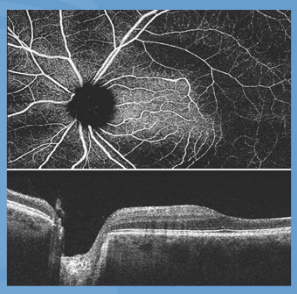


VA: OD: 20/20 OS: 20/200 temporally



Case 10

- Differential?



Case 10 Synopsis

- Susac Syndrome:
  - Rare syndrome which includes encephalopathy, branch retinal artery occlusions, and inner ear disease
- Branch retinal artery occlusion or branch retinal vein occlusions can look like arcuate scotomas

Case 11

- 50-year-old Asian female
- Family history: unsure
- Denies trauma, steroid use
- TMax: 14 mm Hg and 27 mm Hg
- CCT: 521 µm and 529 µm
- Gonioscopy: steep approach, PAS present both eyes

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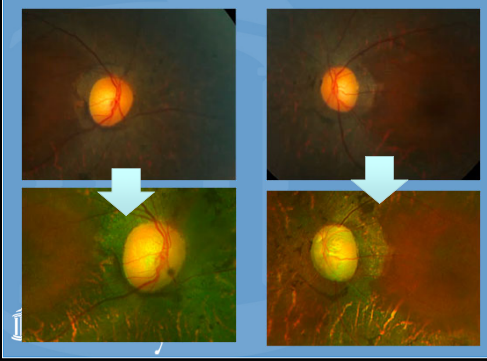
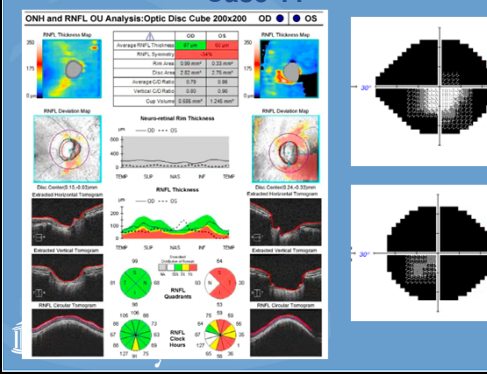
Case 11



Case 11



Case 11 Synopsis

- Retinitis pigmentosa: diffuse progressive dysfunction of rod photoreceptors, then cone photoreceptors and RPE
- Migration of retinal pigment into the anterior chamber has been suggested as a cause of RP-associated glaucoma (open angle mechanisms)
- However, RP may be associated with ACG in rare instances
  - Visual fields and OCT are difficult to interpret in these cases

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Features Suggesting Non-Glaucomatous Diagnosis

History	*Young age*
	Rapid onset
	Rapid progression
	Headache (other than typical migraine)
	Other neurologic symptoms
Exam	Loss of visual acuity or visual field out of proportion to cupping
	Severe dyschromatopsia
	Afferent pupillary defect without significant asymmetry of cupping
	Ocular motility or other neurologic defects
Visual field	Atypical visual field: temporal > nasal, respect of vertical meridian, inferior altitudinal defect, central scotoma
Optic disk	Pallor of preserved rim

Moster M, Kay M. Glaucoma: The Neuro-ophthalmic differential Diagnosis. *J Curr Glaucoma Pract* Jan-Apr 2008;2(1):33-38.

Features Suggesting Non-Glaucomatous Diagnosis

Differentiation of Compressive from Glaucomatous Optic Neuropathy with Spectral-Domain Optical Coherence Tomography

Conclusions: Compressive optic neuropathy is associated with significantly thinner nasal and temporal sectors compared with OAG, whereas OAG results in larger cups and cup volume with OCT measurements. The Heidelberg retinal tomograph is not able to differentiate CON from normal discs. *Ophthalmology 2014;121:1516-1523 © 2014 by the American Academy of Ophthalmology.*

angle glaucoma (OAG) using spectral-domain (SD) optical coherence tomography (OCT) and Heidelberg retinal tomograph (HRT) (Heidelberg Engineering GmbH, Heidelberg, Germany).

Design: Cross-sectional, observational study.

Participants: A total of 200 eyes from 123 patients with CON (69 eyes) or OAG (58 eyes) and controls (73 eyes).

Methods: Univariate and multivariate analyses of HRT parameters, SD-OCT circumpapillary retinal nerve fiber layer (RNFL) thickness, and optic nerve head (ONH) parameters.

Main Outcome Measures: Circumpapillary RNFL, OCT ONH parameters, and HRT parameters.

Results: The univariate analysis of OCT parameters demonstrated significant differences between the temporal and nasal quadrants; clock hours 3 (55 vs. 73 μm), 4, 8 (93.9 vs. 70.7 μm), 9, and 10; vertical cup-to-disc ratio (C:D) (0.6 vs. 0.8) and cup volume (0.2 vs. 0.5) ($P<0.001$) between patients with CON and OAG, respectively. The CON discs were significantly different from normal discs for all OCT parameters except cup volume. The CON discs were not significantly different from normal discs for HRT parameters, except for mean RNFL thickness and cup shape measure. The OAG discs were significantly different from normal discs in all HRT and OCT parameters ($P<0.001$). Multivariate analysis demonstrated that the OCT 3 o'clock temporal sector, average C:D ratio, vertical C:D ratio, and cup volume measurements were able to differentiate OAG from CON.

Conclusions: Compressive optic neuropathy is associated with significantly thinner nasal and temporal sectors compared with OAG, whereas OAG results in larger cups and cup volume with OCT measurements. The Heidelberg retinal tomograph is not able to differentiate CON from normal discs. *Ophthalmology 2014;121:1516-1523 © 2014 by the American Academy of Ophthalmology.*

Features Suggesting Non-Glaucomatous Diagnosis

The Cupped Disc

Who Needs Neuroimaging?

David S. Greenfield, MD,[1] R. Michael Siatkowski, MD,[1] Joel S. Glaser, MD,[1-2] Norman J. Schatz, MD,[1-2] Richard K. Parrish II, MD[1]

Conclusions: Anterior visual pathway compression is an uncommon finding in the neuroradiologic evaluation of patients with a presumptive diagnosis of normal-tension glaucoma. Younger age, lower levels of visual acuity, vertically aligned visual field defects, and neuroretinal rim pallor may increase the likelihood of identifying an intracranial mass lesion. *Ophthalmology 1998;105:1866–1874*

Intervention: The medical records of consecutive glaucoma patients with normal intraocular pressure who underwent brain magnetic resonance imaging or computed tomography scanning as part of a diagnostic evaluation between January 1, 1985, and July 1, 1995, were reviewed. A masked reading of optic nerve photographs and visual fields was performed by one observer. A similar analysis was performed on a control group of consecutive patients with nonglaucomatous optic nerve cupping with known intracranial mass lesions.

Main Outcome Measures: The neuroradiologic findings, clinical characteristics, optic nerve head appearance, and patterns of visual field loss were compared between groups.

Results: None of the patients diagnosed with glaucoma had neuroradiologic evidence of a mass lesion involving the anterior visual pathway. Compared to control subjects, patients with glaucoma were older ($P = 0.0001$), had better visual acuity ($P = 0.002$), greater vertical loss of neuroretinal rim tissue ($P = 0.0001$), more frequent optic disc hemorrhages ($P = 0.01$), less neuroretinal rim pallor ($P = 0.0001$), and more nerve fiber bundle visual field defects aligned at the horizontal midline ($P = 0.0001$). Visual acuity less than 20/40, vertically aligned visual field defects, optic nerve pallor in excess of cupping, and age younger than 50 years were 77%, 81%, 90%, and 93% specific for nonglaucomatous cupping associated with compressive lesions, respectively.

Conclusions: Anterior visual pathway compression is an uncommon finding in the neuroradiologic evaluation of patients with a presumptive diagnosis of normal-tension glaucoma. Younger age, lower levels of visual acuity, vertically aligned visual field defects, and neuroretinal rim pallor may increase the likelihood of identifying an intracranial mass lesion. *Ophthalmology 1998;105:1866–1874*

Conclusions

- OCT RNFL and visual fields are powerful tools in diagnosing and managing glaucoma
- Pattern recognition of OCT – vertical thinning with corresponding visual field defects that respect the raphe – is a key skill to learn
- But: Be aware of conditions that can complicate the interpretation of these tests

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